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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,201	04/02/2002	Michael Chopp	1059.00063	4921

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Kenneth I Kohn
Kohn & Associates
Suite 410
30500 Northwestern Highway
Farmington Hills, MI 48334

EXAMINER	
GEMBEH, SHIRLEY V	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 04/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,201	CHOPP ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *19 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 December 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12 Aug 2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on **19 May 2004** has been entered.

Claims 1-3 and 6-8 were amended. Claims 1-8 are examined as indicated below.

Drawings

The corrected drawings were required in reply to the Office Action mailed 26 Jun 2003. No apparent corrected drawings have been filed. New corrected drawings as previously requested are still required. See PTO-948 for Draftsperson's Patent Drawing Review sent as part of a prior Office Action. Applicant was advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> "The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention."

Claims 1 and 5 – 8 are rejected under 35 U.S.C. 112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1 and 5 - 8 contain Markush claim language that is not closed but should be since it is not clear what is or is not included via the consisting essentially of terminology. See "... selected from the group consisting essentially of ..." where the "essentially of" should be deleted from the claims.

Claim Rejections – 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2 - 5 are rejected under 35 U.S.C. 102(b) as anticipated by Moskowitz US 5385940. Claim 2 requires the neuron growth promoting compound to be a nitric oxide donor; claim 3 requires a pharmaceutical carrier; claim 4 recites augmentation in tissue; and, claim 5 recites L-arginine as on such neurogenesis promoter. These claims are directed to a compound and composition. The intended use – promoting neuron growth – does not alter the compound nor the composition. The Moskowitz patent discloses L-arginine (see, e.g., the abstract, column 3) as a nitric oxide releasing compound. Consequently, the reference anticipates the claimed invention defined in claims 2-5.

Comments in the response unpersuasive

In the response filed 19 May 2004, the remarks and cited decisions at pages 4-12 have been considered but are unpersuasive as to the currently pending claims. As to meeting every element of the claimed invention, note that the compound is taught as a compound for treating stroke the same as in the claims. The compound arginine recited in the claims is the same as in the reference. Thus, citation of *Hybritech Inc. v. Monoclonal Antibodies* and *Richardson c. Suzuki Motor Co., Ltd.* are unpersuasive. It also noted that at pages 5-12 the response, the argument is directed to a method of use. The currently rejected claims above are directed to the compound/composition claims. Method of use arguments are unpersuasive regarding claims directed to compounds and/or compositions.

At page 7 of the response, there is reference to a declaration by inventor Chopp but the argument is directed to the method of use, not to the compound and composition. The declaration is also not executed. Thus, the declaration is unpersuasive as to the claimed compound and composition.

Response page 7 also refers to *Ex parte McCullom, ACS Hospital Systems, Inc. v. Montefiore Hospital, and Ashland Oil, Inc. v. Delta Resins and Refractoris, Inc. et al.* as standing for hornbook law, combining references, and obviousness. In this instance, the argument is unpersuasive. The rejection is one of anticipation, not obviousness.

Of note is that rejected claims 2-5 read on a compound and a composition where L arginine meets the criterion of the claimed compound and the composition. The compound/composition and its properties are inseparable.

Claims 2, 3 and 4 are rejected under 35 U.S.C. 102(b) as anticipated Hindley et.al J. Neuroscience of Research 47:427-439, a compound from claim 1 for promoting neuron growth comprising an effective amount of NO donor sufficient to promote neurogenesis. Hindley et.al. teaches in the abstract that cell cultures treated with NO donors such as Na-nitropruside contained a greater proportion of cell bearing neutrites. Sodium nitroprusside is a known NO donor

Claim 2 is rejected under 35 U.S.C. 102(b) as anticipated by either of Nielsen et.al Am. J. of Crit. Care Med. Vol1611154-1160 (2000) or Poluha et al. Journal of Biological Chem. Vol. 272:38 24002-07.

Nielsen teaches that these compounds can be used as alternatives in administering NO donors in the clinical arena that such drugs are equally effective in the treatment of pulmonary hypertension. In the alternative, and as a separate rejection of claim 2, Poluha teaches at column 2 paragraph 1 that NO is a regulatory molecule that influences many processes, including neuronal proliferation and differentiation, that NO acts as a regulator of cell proliferation which in turn influences process outgrowth.

Claim 5 rejected under 35 U.S.C. 102(b) as anticipated by Schipp et al. Invert Neurosci 4:9-15 1999. Schipp et al. teach that the transmitter NO, is involved in regulation of the vastonus when NO donors/precursors such as phosphodiesterase inhibitors are used at page 10.

Claim Rejections - 35 USC § 103

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moskowitz US 5385940, taken with Poluha et al. Journal of Biological Chem. Vol. 272:38 24002-07, and Adams et al. US 6,284763.

Moskowitz teaches the method of administering the drug can be delivered in any way such as intravascular infusion column 2 line 46. In the specification it is mentioned that the compound can be administered in various ways (page 9 of spec) such as intravenous infusion. Moskowitz also teaches that l-arginine is a NO donor, however it does not *per se* teach the promotion of neural growth, the result however is known to give an outgrowth of neuron as taught by Poluha et al. which is cited here to show a fact, namely that administering NO is known prior to the time the claimed invention was made, to result in neural outgrowth in cells. Thus, one of ordinary skill in the art would

have been motivated to have added NO to promote neural outgrowth as a well as for treatment of stroke where neurological impairment is a noted result (Moskowitz column 1, lines 10-30). The term patient in the claim can be taken to mean any mammalian patient as described in column 2 line 33 of Moskowitz. It is mentioned that the compound is administered to someone who has had a stroke or administered post stroke (column 3, lines 39+). Moskowitz teaches that L-arginine can be administered to a stroke patient, either before, during, or after the stroke column 2 line 19.

While Moskowitz et al. at (column 3, lines 44+) refer to routes of administration that include topical one of ordinary skill in the art would have been aware of and known NO is delivered to various sites needing "augmentation" (sites needing neural outgrowth or increased neurological function). Here, as combined, Adams et al. teaches that systematic routes for administering NO can be through oral, parenteral, intracisternal, transcutaneus (by injection or by patch) intravenous, intramuscular, buccal, or oral spray column 7 line 30. Adams et al also teaches that in a preferred embodiment a method of reversing pathologenic vascular degradative modeling in the ilio-hypogastric-prudendal arterial bed and genitalia NO donors and phosphodiesterase inhibitors can be administered to a patient in need (abstract). Here, one of ordinary skill in the art would have combined the teachings in the Moskowitz reference (col 2, lines 5+) that "the nitric oxide releasing compound is L-arginine. L-arginine is a precursor for nitric oxide synthase, which transforms arginine into NO and citrulline", with that of Poluha et al. which teaches NO administration results in neural proliferation (page 24002, left column) with Adams et al, (abstract) and demonstrates the result of NO administration

as taught by Moskowitz. Thus, the claimed invention was prima facie obvious to make and use at the time it was made.

Claim7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moskowitz US 5385940, taken with Poluha et al. Journal of Biological Chem. Vol. 272:38 24002-07, and Adams et al. US 6,284763 as applied to claims1 and 6 above, and further in view of. Van Waqenen.

Moskowitz, Poluha et al, and Adams are applied here as indicated above from the immediately preceding rejection. In addition where claims 7 and 8, refer to increased neurological function via neuron growth. One of ordinary skill in the art would also have found it obvious to combine the Moskowitz, Poluha et al., and Adams et al. teachings administering NO to effect neural growth with those of Van Wagenen et al. because Van Wagenen et al. teach that growth cones are the motile tips of outgrowing axons and dendrites that serve as both sensory and motor function because stimuli that influence filopdial length, number, and mortality are likely to affect neuronal path finding and that of Thompson teachings that topical l-arginine is a sensitizing agent produced from intracellular nitric acid, which is a potent vasodilator of smooth muscles. Thus, the claimed invention was prima facie obvious to make and use at the time it was made.

No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for all telefax communication to the USPTO is: Official Fax No: (703) 872 9306.

SVG

28 March 28, 2005

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600